UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/976,219	10/12/2001	Yat Sun Or	ENP-030	9357

360'78 7590 07/16/2003

ENANTA PHARMACEUTICALS, INC.
ATTN: PATENT DEPT.
500 ARSENAL STREET
WATERTOWN, MA 02472

EXAMINER
LIU, SAMUEL W

ART UNIT	PAPER NUMBER
1653	11

DATE MAILED: 07/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/976,219	OR ET AL.	
	Examin r	Art Unit	
	Samuel W Liu	1653	

-- The MAILING DATE of this communication app ars on the cover sh t with the corr spondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *5-10,12-14,17 and 18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,11,15,16 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The response filed 9 June 2003 (Paper No. 9) as to amendment of claim 4 and addition of new claims 15-19 have been entered. Because applicants made the additional election with regard to "Y' moiety as (2'-Br)Ph of the claim cyclosporin analog, and because claim 17 is directed to non-elected moiety: Y = (2'-Me)Ph and claim 18 to the substituents other than (2'-Me)Ph, claims 17 and 18 along with claims 5-10 and 12-14 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Thus, the following Office action is applicable to the pending claims 1-4, 11, 15-16 and 19 are examined in this Office action.

Note that the grounds of objection and/or rejection not explicitly stated and/or set forth below are withdrawn.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 11, 15 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Bollinger, P. *et al.* (EP 0296122).

Bollinger *et al.* teach a cyclosporin structure that meets the limitations of the Formula (I) structure of claim 1 of the instant application (see Bollinger et al., formula (II) at page 5 wherein "B" is α-Abu, "X" is Sar, "Y" is Val, and "A" is described by Bollinger's formula (XIX) (see

line 61, page 19) wherein "R_6" group in the formula XIX has the meaning given for Bollinger's formula (V) (see the second line, page 20). Bollinger et al. teach that, in the formula (V), preferred "R_6" group is phenyl (see page 8, line 40). Because Applicant elects "B" as -α-amino butyric acid, "U" as –(D) alanine and "X' as absent for patent examination for the application claims 1-3, Bollinger et al. teaching meets the limitation set forth in the claims.

Bollinger et al. teach R_6" group is *preferably* phenyl-(C_{1-4} alkyl) (see page 8, line 40), which meets the limitation with regard to aryl substituted with C_{1-3} alkyl at "Y" moiety in claim 15. Together with the Bollinger et al. teaching stated above, Bollinger's patent anticipates the application claim 15.

Further, Bollinger et al. teach a pharmaceutical composition comprising the disclosed cyclosporin analog and ingredient for formulation of the composition (see lines 38-64, page 33, and lines 13-50, page 34), as applied to claims 11 and 19 of the current application.

Therefore, Bollinger et al. anticipate claims 1-3, 11, 15 and 19 of the current application.

Response to the rejection under 35 USC 102(b)

The response filed 6 June 2003 commends the issue regarding R_6 group halogen substituents and asserts that there are a large number of the substituents toward R_6 group in the Bollinger et al. reference, and that Bollinger et al. does not describe that the preferred substitution is phenyl group (see page 19, the last two paragraphs). The applicant's argument is found not persuasive because Bollinger et al. teach that especially preferred R_6 group is phenyl and derivative thereof (se page 8, line 40) which is subject to halogen substitution (see page 8, lines 34-36).

Claim Rejections - 35 USC §103

This a new ground of rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4, 11, 15-16 and 19 are rejected under 35 U.S.C. 103(a) as being obvious over Bollinger, P. *et al.* (EP 0296122).

Bollinger *et al.* teach a cyclosporin structure that meets the limitations of the Formula (I) structure of claim 1 of the instant application (see Bollinger et al., formula (II) at page 5 wherein "B" is α-Abu, "X" is Sar, "Y" is Val, and "A" is described by Bollinger's formula (XIX) (see line 61, page 19) wherein "R_6" group in the formula XIX has the meaning given for Bollinger's formula (V) (see the second line, page 20). Bollinger et al. teach that, in the formula (V), preferred "R_6" group is phenyl (see page 8, line 40). Because Applicant elects "B" as -α-amino butyric acid, "U" as –(D) alanine and "X' as absent for patent examination for the application

claims 1-3, Bollinger et al. teaching meets the limitation set forth in the claims. Also, Bollinger et al. teach R_6" group is *preferably* phenyl-(C_{1-4} alkyl) (see page 8, line 40), which meets the limitation with regard to aryl substituted with C_{1-3} alkyl at "Y" moiety in claim 15. Further, Bollinger et al. teach a pharmaceutical composition comprising the disclosed cyclosporin analog and ingredient for formulation of the composition (see lines 38-64, page 33, and lines 13-50, page 34), as applied to claims 11 and 19 of the current application.

Although Bollinger et al. do not explicitly teach (2'-Br)Ph at position "Y" (claim 4) and phenyl substituents at the *ortho* position of the claimed cyclosporin analog (claim 16), the Bollinger et al. teaching is obvious over the application claims 4 and 16. This is because Bollinger et al. teach that phenyl in R_6 group of class I cyclosporin that acts as a pharmaceutical is especially preferred (see the title of the Bollinger's invention which set forth use of cyclosporin as pharmaceutical, and see page 8, lines 40), and that phenyl group is suitable for bearing further substituents, *e.g.*, halogen modification (see page 8, lines 34-35), and because the instant claims are directed to a pharmaceutical salt of the cyclosporin thereof, and the current application, however, does not expressly set forth pharmaceutical importance of the phenyl group modification at *ortho* position in the cyclosporin analog. Thus, halogen substitution at *ortho* position in phenyl group is obvious over the cited art.

One of ordinary skill in the art would have readily made bromine-phenyl substitution at the indicated "Y' moiety of the cyclosporin, and tested for the substituents at *ortho*, or *meta* or *para* position with bromine since bromine substitution is the most common halogen substitution reaction (see the reference labeled as "REF 1", page 1), and would have arrived at the instant

invention with regard to use of cyclosporin analog as a pharmaceutical. Thus, the claimed invention was *prima facie* obvious to make and use at the time it was made.

Provisional Rejection - Obviousness Type Double Patenting

Note that since the response file 9 June 2003 doe not argue against the previous rejection obviousness type double patenting, the rejection is maintained and reiterated in the following.

Claims 1-3 and 11 of this application conflict with Claims 1-3 and 9 of Application No. 09975923 and claims 1-3 and 8 Application No. 09800856. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground

provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130 (b). Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 and 11 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-3 and 9 of copending Application No. 09975293. This is a provisional double patenting rejection because the conflicting claims have not in fact been patented.

Claim 1 of Application 09975923 [see formula I] discloses a cyclosporin analog that is an obvious structural variation of that set forth in the claim 1 [formula (A1)] of the current application. In formula (I) of 09975923, moiety of "A" is an obvious structural variation over the moiety of "A" set forth in formula (I) of the present application in that, provided that "Y" is a functional group, *e.g.*, aryl, and "X" is absent, moiety "B" and "U" are identical for Application 09975923 and the current application.

Claim 2 of Application 09975923 and claim 2 of the present application is identical.

Claim 3 of Application 09975923 and claim 3 of the present application disclose the common subject matter but with different scope with regard to "Y" moiety.

Claim 9 of Application 09975923 and claim 11 of the instant application are identical.

Therefore, the instant application and copending application claims are obvious variation. The claims of the present application are not patentably distinct from the claims of Application 09975923.

Claims 1-3 and 11 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-3 and 8 of copending Application No. 09800856. This is a provisional double patenting rejection because the conflicting claims have not in fact been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application since the referenced copending application and the instant application are claiming common subject matter, as follows:

Claim 1 of Application 09800856 [see formula I] discloses a cyclosporin analog that is an obvious structural variation of that set forth in the claim 1 [see formula (1)] of the current application. In formula I of 09800856, moiety of "A" is the same as moiety of "A1" set forth in formula (1) of the present application in that, provided that "Y" is a functional group, *i.e.*, aryl, "X" is absent, moiety "B" and moiety "U" are identical for Application 09800856 and the current application.

Claims 2-3 of the Application 09800856 and claims 2-3 of the current application disclose the common subject matter but with different scope in regard to the "Y" moiety.

Claim 8 of the Application 09800856 and claim 11 of the current application set forth the common subject matter as to a pharmaceutical composition comprising a cyclosporin compound or/and a pharmaceutically acceptable carrier.

Therefore, the instant application and copending application claims are obvious variation. The claims of the present application are not patentably distinct from the claims of Application 09800856.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is (703) 306-3483. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 703 308-2923. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

Samuel Wei Liu, Ph.D.

January 14, 2003

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER